

REMARKS

Claims 1-32, 36-38, 45, 48, 61-63 are canceled. Claims 49-52 and 54-57 are withdrawn. Claims 33, 34, 35, 39-44, 46, 47, 58-60 and 64-66 are amended, as discussed below. New claims 67, 68 and 69 are added. Support for the new claims is found in the specification as originally filed, including at page 26. It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. Claim Objections

Claims 34, 35, 37-47, 49-57, 60 and 62-66 are objected to for various reasons.

Claims 34, 35, 37-47, 49-57 and 66 are objected to for the inconsistent reference to the cutinase variants. Appropriate correction has been made to the claims to use more consistent terminology.

Claims 41, 42, and 46 are objected to on the basis that there is no space between "in" and "SEQ ID NO:1". The claims have been amended to correct this typographical error.

Claim 35 is objected to on the basis that the organism "*H. insolens*" should be spelled out. Claim 35 has been amended accordingly.

Claims 35 and 60 are objected to as not properly further limiting the subject matter of the claims from which they depend. The Examiner states that claims 33 and 59 recite that the cutinase variants have 80% homology to the reference sequence whereas claims 35 and 60 recite that the cutinase variant is a variant of a cutinase from *H. insolens*.

The Examiner objection is clearly not valid. Claims 35 and 60 are narrower than claims 33 and 59. Claims 33 and 59 do not require that the parent enzyme must be the *H. insolens* parent. A proper dependent claim is one that is narrower than the claim from which it depends. Thus, Claims 35 and 60 clearly fulfill this requirement.

Claim 59, with dependent claims 60 and 62-65, are objected to as being drawn to non-elected inventions. Applicants believe the Examiner is mistaken. Claims 59, 60 and 62-65 have already been examined. See, e.g., the Examiner's Office Action of November 3, 2003. The Examiner is requested to withdraw this objection as it is not consistent with the record.

II. Enablement Rejection

Claims 33-35, 37, 38, 40-47, 49-60, 62, 63, 65 and 66 are rejected under 35 U.S.C. 112, as lacking enablement. The Examiner contends that the specification does not reasonably provide enablement for cutinase variants that have above 80%, above 85%, or above 90% homology to SEQ ID NO:1. This rejection is respectfully traversed.

The claims have been amended to expedite prosecution by reciting that the variant has above 90% homology to SEQ ID NO:1. As discussed below, applying the Wands factors clearly shows that the claimed invention is enabled.

As summarized by the Federal Circuit in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), the factors to be considered in determining whether undue experimentation is required include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the relative skill of those in the art (7) the predictability in the art and (8) the breadth of the claims.

The Examiner is respectfully directed to Example 2 of the specification. Example 2 describes many cutinase variants following within the scope of the new claims which are less than 95% homology to SEQ ID NO:1, including cutinase variants having 9 substitutions and an N-terminal extension of 17 amino acids, 10 substitutions and an N-terminal extension of 17 amino acids 13 substitutions and an N-terminal extension of 17 amino acids, 11 substitutions and an N-terminal extension of 17 amino acids, and 15 substitutions and an N-terminal extension of 17 amino acids. As indicated by these working examples, the skilled artisan is enabled to make variants that are less than 95% homologous.

It is also noted that the claims are of a very narrow scope, encompassing only a small degree of variation relative to SEQ ID NO:1. In particular, the cutinase variants of the claimed invention are relatively small proteins, as the reference cutinase is only 194 amino acids long, and the claims encompasses variant cutinases which are above 90% homology to SEQ ID NO:1. Thus, the breadth of the claims is very narrow.

The specification and the prior art also provide significant guidance as to how to produce the variants, including other alterations that can be made as well as important conserved amino acids. The specification provides detailed guidance as to how to produce the cutinase variants. See, e.g., the methods described at page 11-12, referring to the methods of random and site directed mutagenesis. The technology available to the artisan at the time of the invention also included random mutagenesis protocols described in WO 95/22615. The Examiner is also directed to U.S. Patent No. 6,815,190, which corresponds to WO 00/34450, published on June 15,

2000. The '190 patent provides the artisan with the atomic coordinates and three dimensional structure for the reference cutinase sequence from *Humicola insolens*. See Figure 1 and col. 3-4. As is well-known in the art, a crystal structure provides important information, including providing insight to which amino acids should be conserved. The '190 patent also provides a list of additional alterations which guide the artisan. See, e.g., col. 3, lines 55-60, col. 4, lines 1-29 and Examples 1-3.

The Examiner is also clearly applying a level of skill that is not representative of the level of skill in the art as of the time of the filing of the invention. The Examiner should appreciate the fact that the level of skill in the applicable art is very high as evidenced, for example, by the art presented in the Background of The Invention, the art cited in the information disclosure statement submitted on November 2, 2001, and the guidance provided in the specification. As of October 2000, persons of ordinary skill in the art were unquestionably able to routinely produce and screen in a short period of time thousands to hundreds of thousands of mutants of a known sequence through mutagenesis and other techniques. The specification provides an extensive disclosure of techniques which are well-known in the art for obtaining cutinases which are 90% homologous to SEQ ID NO:1, and indeed it was routine for persons of ordinary skill in the art at the time of the invention to prepare cutinase variants which possess above 90% homology to SEQ ID NO:1.

In addition to the technology described in the specification for generating variants having a desired activity, the artisan was also able to carryout the gene shuffling protocols of Stemmer (see, e.g., U.S. Patent No. 6,365,408) and other gene diversity protocols. These tools enabled an artisan at the time of the invention to rapidly generate an enormous number of variants having the claimed alterations, having 90% homology to SEQ ID NO:1 and which are functional. Thus, the experimentation necessary to obtain additional variants beyond those described and exemplified in the specification and known in the art was routine to the artisan at the time of the invention and the predictability in obtaining such cutinase was very high.

The Examiner is also requested to consider that the USPTO has previously allowed claims to cutinase variants having about 90% homology to SEQ ID NO:1. See issued claims 1 and 3 of U.S. Patent No. 6,815,190. As this is an earlier filed case, certainly the skill in the art has progressed since this point and it is not clear how the artisan was enabled to produce such variants in 1998, but is now not enabled to produce such variants a few years later.

Thus, as is clear from the above analysis, the claims are enabled for cutinase variants having 90% homology to SEQ ID NO:1. Thus, Applicants submit that the claims overcome this

rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

III. Indefiniteness Rejection

Claims 33-35, 37-47, 49-58 and 66 are rejected under 35 U.S.C. 112, as indefinite.

The Examiner states that use of the term "modification" is confusing because it includes chemical modification and because it is not consistent with the use of the term "substitution" in the dependent claims. In order to be consistent with the dependent claims, Applicants have amended the claims to use the term "substitution."

Claims 41 and 42 are rejected as confusing for using "and/or." The phrase "and/or" means either that all members are included, when using "and", and that all members need not be included, when using "or." However, as the use of the term "or" would encompass the inclusion of other alterations, the claims have been amended to employ the term "or."

Claim 45 is rejected on the basis that there is insufficient antecedent basis for the term "parent cutinase." The cancellation of claim 45 renders this rejection moot.

Claim 46 is rejected as confusing for using the phrase "further comprising." Claim 46 is amended to use the phrase "comprising."

Claim 47 is rejected on the basis that it is unclear how the phrase "wherein the cutinase variant is a variant of a cutinase that has the amino acid sequence of SEQ ID NO:1" because it is unclear how this distinguishes a variant of parent cutinase which has above 80% homology to SEQ ID NO:1. The phrase in claim 47 clearly distinguishes the phrase in claim 33 because claim 33 is not limited to making variants of only the cutinase of SEQ ID NO:1. Thus, claim 33 is narrower in that it requires that the cutinase is a variant of the cutinase of SEQ ID NO:1.

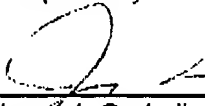
For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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